SHORT COMMUNICATION

SCNN1, an Epithelial Cell Sodium Channel Gene in the Conserved Linkage Group on Mouse Chromosome 6 and Human Chromosome 12

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SCNN1, a gene encoding a nonvoltage-gated sodium channel, was detected using a rat colon cDNA probe with homology to Caenorhabditis elegans degenerin genes. Human SCNN1 was assigned to chromosome 12 using the NIGMS hybrid mapping panel 2. Mouse SCNN1 was mapped to a conserved linkage group on distal chromosome 6. The observed order of mouse genes was centromere–Raf1 (2.1±2.1)–Senn1, Vuf–(1.9±1.9)–Ntf3, with 0/101 recombinants between Senn1 and Vuf. No rearrangements of genomic DNA were detected in the linked mouse mutations deaf waddler (dfw) and opisthotonus (opt). © 1994 Academic Press, Inc.

cDNAs encoding an epithelial, nonvoltage-gated, amiloride-sensitive sodium channel were recently isolated from rat colon and human lung cDNA libraries (2, 6, 10). Expression of the rat cDNA clone arENaC in Xenopus oocytes resulted in generation of an amiloride-sensitive sodium current (2). The rat cDNA shares significant sequence homology with two degenerin genes from Caenorhabditis elegans, mec-4 and deg-1. Mutations in mec-4 and deg-1 result in degeneration of specific neurons. To determine the potential relationship of this cation channel gene to known mouse mutants, we have mapped the mouse homology.

To expedite localization of the mouse gene, a human/rodent somatic cell hybrid panel was first analyzed. The 2.1-kb SacI fragment of the rat arENaC cDNA (2) was used to probe genomic DNA from the NIGMS human/rodent somatic cell hybrid mapping panel 2 (Cornell Institute for Medical Research, Camden, NJ). Species-specific HinfI restriction fragments of 18, 5.5, and 5.1 kb were detected in human genomic DNA (Fig. 1A). These fragments were also detected in cell line GM 10862, which contains human chromosome 12 as the only human chromosome. All of the other hybrids in this panel were negative, indicating that the human locus, designated SCNN1 (sodium channel, nonvoltage-gated 1; gene symbol reserved), is located on chromosome 12. No additional cross-hybridizing human fragments were detected when the temperature was reduced to 55°C, suggesting that there may be no other closely related genes in the mammalian genome. The assignment to chromosome 12 is consistent with the results of in situ hybridization reported while the manuscript was in preparation (10).

Homologs of loci from human chromosome 12 are present in three large linkage groups on mouse chromosomes 6, 10, and 15 (3). To determine whether the mouse Senn1 gene is part of the linkage group on chromosome 6, we analyzed two mapping panels that were previously typed for markers on this chromosome (1, 5). Restriction fragment length polymorphisms were identified by hybridization of the arENaC cDNA to blots containing genomic DNA from strains C57BL/6J, SPRET/Ei, and CAST/Ei that was digested with eight restriction endonucleases. In addition to several invariant bands, we observed a 1.3-kb PstI fragment specific to strain CAST/Ei and a 17-kb BglII fragment specific to strain SPRET/Ei (data not shown). These fragments were analyzed in DNA from the two chromosome 6 mapping panels. The results were consistent and demonstrated close linkage (0/101 recombinants) between Senn1 and Vuf (Fig. 1B). The indicated gene order from the CAST F2 is centromere–D6Mit8 (12.5±4.8)–Raf1, D6Mit11 (2.1±2.1)–Senn1, Vuf, D6Mit12 (10.4±4.4)–D6Mit14. The distance between Senn1 and neurotrophin 3 (Ntf3), also found on human 12p13, was determined on the BSB backcross with the following results: centromere–D6Mit8 (7.5±3.6)–mi (9.4±4.0)–Senn1, Vuf, D6Mit12 (1.9±1.9)–Ntf3. The gene order indicated by the two crosses is combined in Fig. 1C.

Senn1 mapped to the same region of chromosome 6 as two mutants with neurological disorders, deaf waddler (dfw) and opisthotonus (opt) (4, 8). To determine whether Senn1 is rearranged in either mutant, genomic DNA samples were obtained from The Jackson Laboratory (Bar Harbor, ME). dfw was compared with the strain of origin, C3H/HeJ, and opt was compared
however, the possibility of a more subtle mutation has not been eliminated.

In addition to SCNN1, VWF, and NTF3, 20 other genes have been assigned to the conserved linkage group on human chromosome 12 and distal mouse chromosome 6 (3, 7). Human VWF encoding von Willebrand factor is the most distal gene mapped to chromosome 12p13.3. The close linkage of Scnn1 and Vwf in the mouse indicates that human SCNN1 is likely to be located at the distal terminus of the chromosome arm. This is consistent with the recently reported in situ hybridization of the human lung cDNA to chromosome 12p13 (10).

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REFERENCES


